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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,361	11/26/2003	Yizhong Gu	PB0105	1196

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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	**PAPER NUMBER**
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,361	GU ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *62-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *62-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 62-70 are pending in the application.

[2] Applicant's amendment to the claims, filed on 12/5/06, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Applicant's amendment to the specification, filed on 12/5/06, is acknowledged.

[4] Applicant's arguments filed on 12/5/06 in response to the Office action mailed on 9/5/06 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objection

[6] Claims 62-65 are objected to as being grammatically incorrect in the recitation of "said protein having ATPase activity." It is suggested that the noted phrase be amended to recite "said protein has ATPase activity."

Claim Rejections - 35 USC § 101

[7] Claims 62-66 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a protein of SEQ ID NO:3 and variants thereof. The claims read on a product of nature and should be

amended to indicate the hand of the inventor, e.g., by insertion of "purified" or "isolated." See MPEP § 2105.

[8] Claims 62-70 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or well-established utility. The claims are drawn to SEQ ID NO:3 and variants thereof, and a fusion protein.

The specification discloses SEQ ID NO:3 is a "a human myosin-like protein" (specification at p. 8, middle) or a "human myosin heavy chain-like protein" (specification at p. 15, bottom). According to the specification, defects in SEQ ID NO:3 function and/or expression contribute to human disease (p. 164, bottom) and SEQ ID NO:3 is useful in diagnosis, prevention, or treatment of disorders (specification at p. 15, bottom). However, there is no evidence of record that the polypeptide of SEQ ID NO:3 is a defective polypeptide, is associated with or contributes to human disease, or can be used to diagnose, prevent, or treat a disorder. Thus, without further experimentation, one of skill in the art would not be able to use the claimed polypeptide for these uses. This type of utility is not considered a "substantial utility". See e.g., *Brenner v. Manson,* 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The specification must teach a skilled artisan how to use what is claimed and not merely provide a blueprint for further experimentation in order for an artisan to identify a use for the claimed invention.

[9] Claims 62-70 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial utility

asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

RESPONSE TO ARGUMENT: According to applicant at p. 9 of the instant response, new claims 62-70 are drawn to subject matter not previously rejected under 35 U.S.C. 101 or the how to use requirement of 35 U.S.C. 112, first paragraph and thus the objection is obviated by amendment.

Applicant's argument is not found persuasive. Claims to the polypeptide of SEQ ID NO:3, variants thereof, and a fusion protein were presented in the prior claim amendment filed 6/23/06. See 9/5/06 Office action at p. 4, lines 3-4 of paragraph 10. As such, the basis for rejecting the claims of that amendment is the same as the basis for rejecting newly added claims 62-70, *i.e.*, the claimed invention is not supported by either a specific and substantial asserted utility or well-established utility.

It is noted that if the claimed polypeptide has a well-established utility that has not been disclosed in the instant specification, applicant is requested to state such well-established utility for the examiner's consideration.

Claim Rejections - 35 USC § 112, First Paragraph

[10] Claims 62-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 62-64 (claims 65-70 dependent therefrom) are drawn to (in relevant part) a genus of variants of SEQ ID NO:3 that have at least 90%, 95%, or 99% amino acid sequence identity to SEQ ID NO:3 and have ATPase activity or are capable of binding calmodulin, optionally wherein the protein activity is limited to ATPase activity (claim 65) or is limited to being capable of binding calmodulin (claim 66).

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of the claimed genus of polypeptides, *i.e.*, SEQ ID NO:3. The specification fails to describe any additional representative species of the claimed genus of nucleic acids. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus," it

also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." In the instant case, the claimed genus of polypeptides encompasses species that are widely variant in their structures. For example, the polypeptide of claim 62 allows for up to about 257 amino acid variations and even at 99% identity to SEQ ID NO:3 (a 2568 amino acid polypeptide), claim 64 allows for up to about 25 amino acid variations. Moreover, the genus encompasses species that are widely variant in their functions, as the prior art acknowledges that numerous structurally and functionally diverse proteins bind to calmodulin (Ikura et al., *PNAS* 103:1159-1164, 2006, see particularly p. 1162, left column, bottom). Thus, even claim 64, which is structurally limited to a polypeptide with 99% sequence identity to SEQ ID NO:3 is functionally diverse in view of the prior art's disclosure that "numerous...functionally diverse proteins bind to calmodulin." As such, the disclosure of the single representative species as noted above is insufficient to be representative of the attributes and features of all species of polypeptides as encompassed by the claims.

Given the lack of description of a representative number of polypeptides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

RESPONSE TO ARGUMENT: Applicant argues the rejection is obviated by amendment to cancel the rejected claims and newly presented claims require the protein to have ATPase activity or be capable of binding to calmodulin.

Applicant's argument is not found persuasive. As noted above, the single disclosed species of SEQ ID NO:3 fails to reflect the structural and functional variation among the members of the genus of claimed polypeptides and consequently, the genus of claimed polypeptides lacks adequate written description.

[11] Claims 62-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:3, does not reasonably provide enablement for all variants of SEQ ID NO:3 as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation is required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on

the content of the disclosure. See MPEP § 2164.01(a). MPEP 2164.04 states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: Claims 62-64 (claims 67-70 dependent therefrom) are drawn to (in relevant part) variants of SEQ ID NO:3 that have at least 90%, 95%, or 99% amino acid sequence identity to SEQ ID NO:3 and have ATPase activity or are capable of binding calmodulin, optionally wherein the protein activity is limited to ATPase activity (claim 65) or is limited to being capable of binding calmodulin (claim 66). The enablement provided by the specification is not commensurate in scope with the claims with regard to the variants of SEQ ID NO:3 encompassed by claims 62-66. In this case, the specification is enabling for SEQ ID NO:3.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: As noted in the prior Office action, the amino acid sequence of a polypeptide determines the its structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity/utility requires a knowledge of and guidance with regard to which amino

acids in the protein's sequence, if any, are tolerant of modification and which are conserved (*i.e.*, expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining a polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, *e.g.,* multiple substitutions. At the time of the invention, methods for isolating or generating variants and mutants of a given polypeptide were known in the art. However, neither the specification nor the state of the art at the time of the invention provided the necessary guidance for altering the polypeptide of SEQ ID NO:3 with an expectation of obtaining a polypeptide having the desired activity/utility. At the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity/utility. For example, the reference of Witkowski et al. (*Biochemistry* 38:11643-11650, 1999) teaches that only a single amino acid substitution results in conversion of the activity of a polypeptide to a second, distinct activity (see *e.g.*, Table 1, page 11647). Further, even if one were to isolate variants of SEQ ID NO:3 that were capable of binding calmodulin, as noted above, the prior art recognizes that numerous functionally diverse proteins bind to calmodulin (Ikura et al., *PNAS* 103:1159-1164, 2006, see particularly p. 1162, left column, bottom)

and thus, the polypeptide, while having the capability to bind calmodulin, may have any of a number of functionalities unrelated to ATPase activity.

The amount of direction provided by the inventor and The existence of working examples: The specification discloses only a single working example of the claimed polypeptide, *i.e.,* SEQ ID NO:3. The specification fails to disclose any specific guidance for altering the polypeptide of SEQ ID NO:3 with an expectation that the polypeptide variant will maintain the desired activity/utility. Furthermore, the specification fails to provide any guidance for using those polypeptides that, while maintaining the ability to bind calmodulin, do not maintain the desired ATPase activity, which according Ikura et al. encompasses numerous functionalities that are unrelated to ATPase activity.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating and/or generating variants of a polypeptide were known in the art at the time of the invention, it was not routine in the art to screen – by a trial and error process – for all polypeptides having a substantial number of modifications as encompassed by the claims for those that maintain the desired activity/utility.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, undue experimentation is necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated

with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

RESPONSE TO ARGUMENT: Applicant argues the rejection is obviated by amendment to cancel the rejected claims and to "avoid the phrases which the Examiner objects as impermissibly broadening the claimed genera."

Applicant's argument is not found persuasive. As noted above, the specification fails to enable all variants of the SEQ ID NO:3 as encompassed by the claims without requiring undue experimentation.

Claim Rejections - 35 USC § 102

[12] The rejection of claim(s) 22, 35, 45, 50, and 57-58 under 35 U.S.C. 102(b) as being anticipated by Lehner et al. (WO 96/23886) is withdrawn in view of the amendment to cancel these claims. Further, it is noted that the polypeptide of Lehner et al. does not satisfy the structural limitations of claims 62-64 and thus the reference is not available as prior art under 35 U.S.C. 102.

Conclusion

[13] Status of the claims:

- Claims 62-70 are pending.
- Claims 62-70 are rejected.
- No claim is in condition for allowance.

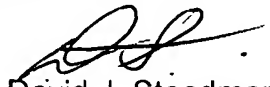
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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Art Unit 1656